CLAIMS

1. A multivalent vaccine comprising at least two recombinant variable regions of immunoglobulin molecules derived from B-cell lymphoma cells, wherein said cells express at least two different immunoglobulin molecules, said immunoglobulin molecules differing by at least one idiotope.

2. The vaccine of Claim 1, wherein said vaccine comprises at least two recombinant immunoglobulin molecules comprising said recombinant variable regions derived from said lymphoma cells.

3. The vaccine of Claim 2, wherein said recombinant immunoglobulin molecules are covalently linked to an immune-enhancing cytokine.

4. The vaccine of Claim 3, wherein said cytokine is selected from the group consisting of granulocyte-macrophage colony stimulating factor, interleukin-2 and interleukin-4.

5. The multivalent vaccine of Claim 1 further comprising at least one pharmaceutically acceptable excipient.

6. The multivalent vaccine of Claim 1 further comprising an adjuvant.

7. A method of producing a vaccine for treatment of B-cell lymphoma comprising:

a) providing:

i) malignant cells isolated from a patient having a B-cell lymphoma;

ii) an amplification vector comprising a recombinant oligonucleotide having a sequence encoding a first inhibitable enzyme operably linked to a heterologous promoter;

iii) a eukaryotic parent cell line;

b) isolating from said malignant cells nucleotide sequences encoding at least one V_H region and at least one V_L region, said V_H and V_L regions derived from immunoglobulin molecules expressed by said malignant cells;

c) inserting said nucleotide sequences encoding said V_H and V_L regions into at least one expression vector;

d) introducing said at least one expression vector and said amplification vector into said parent cell to generate one or more transformed cells;

e) growing said transformed cell in a first aqueous solution containing an inhibitor capable of inhibiting said inhibitable enzyme wherein the concentration of said inhibitor present in said first aqueous solution is sufficient to prevent growth of said parent cell line; and

f) identifying a transformed cell capable of growth in said first aqueous solution, wherein said transformed cell capable of growth expresses said V_H and V_L regions.

8. The methods of Claim 7, wherein transformed cell capable of growth contains an amplified number of copies of said expression vector and an amplified number of copies of said amplification vector.

9. The method of Claim 7, wherein nucleotide sequences encoding said V_H and V_L regions comprise at least two V_H and at least two V_L regions.

10. The method of Claim 7, wherein said parent cell line is a T lymphoid cell line.

11. The method of Claim 7, wherein said parent cell line contains an endogenous gene encoding a second inhibitable enzyme.

12. The method of Claim 11, wherein said second inhibitable enzyme is selected from the group consisting of dihydrofolate reductase, glutamine synthetase, adenosine deaminase, asparagine synthetase.

13. The method of Claim 7, wherein said concentration of inhibitor present in said first aqueous solution is four to six-fold the concentration required to prevent the growth of said parent cell line.

14. The method of Claim 7, wherein said first and said second inhibitable enzyme are the same.

15. The method of Claim 7, further comprising providing a selection vector encoding a selectable gene product which is introduced into said parent cell line together with said expression vector and said amplification vector.

16. The method of Claim 15, wherein said selection vector encodes an active hypoxanthine guanine phosphoribosyltransferase.

17. The method of Claim 16, wherein said aqueous solution which requires the expression of said selectable gene product comprises hypoxanthine and azaserine.

18. The method of Claim 15, further comprising following the introduction of said vectors the additional step of growing said transformed cell in a second aqueous solution which requires the expression of said selectable gene product prior to growing said

transformed cell said first aqueous solution containing an inhibitor capable of inhibiting said inhibitable enzyme.

19. The method of Claim 7, wherein said amplification vector encodes an active enzyme selected from the group consisting of dihydrofolate reductase, glutamine synthetase, adenosine deaminase, asparagine synthetase.

20. The method of Claim 19, wherein said inhibitor is selected from the group consisting of methotrexate, 2'-deoxycoformycin, methionine sulphoximine, albizziin and β-aspartyl hydroxamate.

21. A method of treating B-cell lymphoma, comprising:

a) providing:

i) a subject having a B-cell lymphoma;

ii) a multivalent vaccine comprising at least two recombinant variable regions of immunoglobulin molecules derived from said subjects's B-cell lymphoma cells, wherein said cells express at least two different immunoglobulin molecules, said immunoglobulin molecules differing by at least one idiotope;

b) administering said multivalent vaccine to said subject.

22. The method of Claim 21, wherein said vaccine comprises at least two recombinant immunoglobulin molecules comprising said recombinant variable regions derived from said lymphoma cells.

23. The method of Claim 21, wherein said vaccine further comprises an adjuvant.

24. The method of Claim 22, wherein said adjuvant is Syntex adjuvant formulation 1.